

WHAT IS CLAIMED IS:

1. A process for controlling the amount of sialic acid present on an oligosaccharide side chain of a glycoprotein produced by mammalian cell culture which comprises:  
culturing the mammalian host cell in a production phase of the culture which is characterized by;
  - i) adding an alkanolic acid or a salt thereof to the cell culture at a concentration of about 0.1 mM to about 20 mM; and
  - ii) maintaining the osmolality of the cell culture at about 250 to about 600 mOsm.
2. The process according to claim 1 wherein the amount of sialic acid present on the oligosaccharide side chain of the glycoprotein is increased and wherein;  
cell specific productivity of the cell culture is decreased by culturing the host cell at a concentration of the alkanolic acid or salt thereof of about 0.1 to about 6mM and maintaining the osmolality at about 300-450 mOsm.
3. The process of claim 2 in which the host cell is a CHO cell.
4. The process according to claim 3 wherein the alkanolic acid or salt thereof is sodium butyrate.
5. The process according to claim 4 wherein the glycoprotein produced is a mammalian glycoprotein.
6. The process according to claim 5 wherein the glycoprotein is a tumor necrosis factor receptor-immunoglobulin chimera.

7. The process of claim 6 in which the host cell is a dp12.CHO cell line transfected with the vector carrying the cDNA encoding a soluble type 1 tumor necrosis factor immunoglobulin G<sub>1</sub> chimera.
8. The process according to claim 1 wherein the amount of sialic acid present on the oligosaccharide side chain of the glycoprotein is decreased and wherein; cell specific productivity of the cell culture is increased by culturing the host cell at a concentration of about 6mM to about 12 mM of the alkanolic acid or salt thereof and maintaining the osmolality at about 450-600 mOsm.
9. The process of claim 8 in which the host cell is a CHO cell.
10. The process according to claim 9 wherein the alkanolic acid or salt thereof is sodium butyrate.
11. The process according to claim 10 wherein the glycoprotein produced is a mammalian glycoprotein.
12. The process according to claim 11 wherein the glycoprotein is a tumor necrosis factor receptor-immunoglobulin chimera.
13. The process of claim 14 in which the host cell is a dp12.CHO cell line cell transfected with the vector carrying the cDNA for a soluble type 1 tumor necrosis factor immunoglobulin G<sub>1</sub> TNFR1-IgG<sub>1</sub> chimera.
14. A process for producing a tumor necrosis factor receptor-immunoglobulin TNFR1-IgG<sub>1</sub> chimeric protein comprising;

- (a) culturing a mammalian host cell which expresses a TNFR-IG chimera in a growth phase under such conditions and for a period of time such that maximum cell growth is achieved;
  - (b) culturing the host cell in a production phase in the presence of sodium butyrate at a concentration of about 6mM to about 12 mM;
  - (c) maintaining the osmolality of the production phase at about 450-600 mOsm.
15. A process for producing a tumor necrosis factor receptor-immunoglobulin TNFR1-IgG<sub>1</sub> chimeric protein comprising;
- (a) culturing a mammalian host cell which expresses a TNFR-IG chimera in a growth phase under such conditions and for a period of time such that maximum cell growth is achieved;
  - (b) culturing the host cell in a production phase in the presence of sodium butyrate at a concentration of about 1mM to about 6 mM;
  - (c) maintaining the osmolality of the production phase at about 300-450 mOsm.
16. The process of claim 15 in which the host cell is a CHO cell.
17. The process of claim 16 in which the host cell is a dp12.CHO line.
18. A preparation comprising the TNFR1-IgG<sub>1</sub> produced by the process of claim 17.
19. A therapeutic composition comprising the TNFR1-IgG<sub>1</sub> produced by the process of claim 15, and a pharmaceutically acceptable excipient.

20. A TNFR1-IgG1 preparation comprising TNFR1-IgG1 molecules wherein the TNFR1-IgG1 molecules have a molar ratio of sialic acid to protein of about 4-7.
21. A TNFR1-IgG1 preparation comprising TNFR1-IgG1 molecules wherein the TNFR1-IgG1 molecules have about 1-2 moles of exposed N-acetylglucosamine residues per mole of TNFR1-IgG1 protein.
22. A TNFR1-IgG1 preparation comprising TNFR1-IgG1 molecules wherein the TNFR1-IgG1 molecules have a molar ratio of sialic acid to N-acetylglucosamine of about 0.35 to about 0.5.
23. The TNFR1-IgG1 preparation of claim 22 wherein the molar ration of sialic acid to N-acetylglucosamine is about 0.39 to about 0.45.